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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,477	11/21/2003	Lieping Chen	07039-443001	3624

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EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,477	CHEN ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 32-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment/remarks, filed 05/08/2006, are acknowledged.

Claims 1 – 39 are pending.

2. Applicant's election with traverse of Group III (claims 19 – 24, drawn to a method of diagnosis, comprising detecting B7-H1-specific antibodies in a body fluid) in the reply filed on 05/08/2006 is acknowledged.

The traversal is on the grounds that the methods of Groups III and IV (claims 25 – 31, drawn to a method of monitoring the progress of a disease, comprising measuring the level of B7-H1-specific antibodies in a body fluid) are closely related.

In view of Applicant's argument, the restriction requirement between groups III and IV has been withdrawn.

Applicant further elected the Species of rheumatoid arthritis as the autoimmune disease. In the interest of compact prosecution, examination has been extended to include all Species of autoimmune disease.

3. Claims 1 – 18 and 32 – 39 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

Claims 19 – 31 are under consideration in the instant application.

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The provisional application USSN 60/428,132 upon which priority is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. It is noted that apparently no IDS has been filed in the instant application.

7. The use of trademarks has been noted in this application (e.g. Biacore on page 14). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

8. Claim 19 is objected to because of the following informalities: in the recitation of "wherein an elevated level of one more B7-H1-specific antibodies," it appears that "one or more" has been intended. Appropriate correction is required.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 19 – 31 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 19 – 31 are indefinite in the recitation of "identifying a subject that is suspected of having, or is likely to develop, a disease," because the criteria for "identification" are unknown. The term is not defined by the claim, and the specification appears to be silent as to how the identification is to be accomplished, other than to indicate that it can be done "by methods known in the art" (page 12 line 6). However, one of ordinary skill in the art would not be reasonably apprised as to which of the various methods known in the art are encompassed by the instant claims.

B. Claims 19 – 24 are indefinite in the recitation of "an elevated level of one or more B7-H1-specific antibodies," because "elevated" is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of elevation or base level for comparison, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

C. Claims 25 – 31 are indefinite in the recitation of "wherein the level of one or more B7-H1-specific antibodies in the sample correlates with the stage of the disease or pathological condition," because the phrase is vague and indefinite. In the absence of a specific recitation, one of ordinary skill in the art would not be reasonably apprised of which level of the antibody would "correlate" with which stage of the disease, or of the amount or degree of any such "correlation."

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 19 – 31 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The following *Written Description* rejection is set forth herein.

Applicant is not in possession of antibodies to a genericallly recited "B7-H1."

The specification does not sufficiently define the term "B7-H1," nor does it provide sufficient structural or functional description of the molecule. Therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities encompassed by the instant claims.

A description of a genus of protein sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. Claims 19 – 31 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

The specification does not provide a sufficient enabling description of the claimed methods of diagnosis of rheumatoid arthritis (RA), or monitoring the progress of RA.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses at pages 41 – 42 (Example 2) that sera from 29% of RA patients contained elevated levels of autoantibodies specific for B7-H1. Thus the method appears to be informative for only a relatively small fraction of RA patients. Conversely, the specification discloses that 4% of health donors were positive for the presence of such antibodies (ibid). When compared to the incidence of RA in population of 0.25 – 0.5% (e.g. Uhlig et al., 2005, Ann. Rheum. Disease, 64: 7 – 10; see entire document, in particular e.g. the Abstract), this high incidence of "false positives" inherent in the claimed method appears to prevent one of skill in the art to practice the invention as claimed without undue experimentation. It is noted that in the absence of a specific definition in the specification as filed, the recitation "a subject that is suspected of having, or is likely to develop" a disease is interpreted broadly to encompass the entire population.

Likewise, the specification discloses at page 42 (Example 3) a relatively small difference between the occurrence of active RA between B7-H1 antibody-positive patients (89%) and B7-H1 antibody-negative patients (56%). In discussing these data, Dong et al. (J. Clin. Investigat., 2003, 111: 363 – 370; see entire document) caution that it is unknown whether or not B7-H1 autoantibodies are correlated with active disease, due to the semiquantitative nature of the ELISA assay used in these studies, and subjective diagnostic standards for active disease (e.g. page 369, second column).

Without sufficient guidance, the relationships between the presence of anti-B7-H1 antibodies and RA, and between the level of anti-B7-H1 antibodies and the stage of RA, are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

14. Claims 19 – 31 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

The specification does not provide a sufficient enabling description of the claimed methods of diagnosis, or of monitoring the progress, of a generically recited "disease or pathological condition" with symptoms caused by activation of T cells, or of "an autoimmune disease," as well as specifically recited systemic lupus erythematosus (SLE) and autoimmune hearing loss.

The specification discloses a correlation between the level of autoantibodies to B7-H1 and the presence of RA or a stage of RA (pages 42 – 43). As discussed in section 13 above, this is not seen as providing sufficient enabling disclosure for the claimed methods as they apply to RA. Neither is the specification seen as providing sufficient enabling disclosure for the claimed methods as they apply to generically recited "disease or pathological condition" with symptoms caused by activation of T cells, or "an autoimmune disease," especially in view of the limited direction or guidance provided by the Applicant, absence of working examples applicable to other diseases, the unpredictability in the art.

In reviewing the unpredictability of assessment of SLE using biomarkers, including autoantibodies, Merrill et al. (Best Practice and Research Clinical Rheumatology, 2005, 19: 709 – 726; see entire document) note that to date, "not a single candidate biomarker has been uniformly and rigorously validated for any aspect of SLE" (page 712 second paragraph). Therefore, the amount of experimentation required to enable one of skill in the art to practice the claimed invention is unnecessarily, and improperly, extensive and undue.

15. Conclusion: no claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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July 3, 2006

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1644
7/3/06